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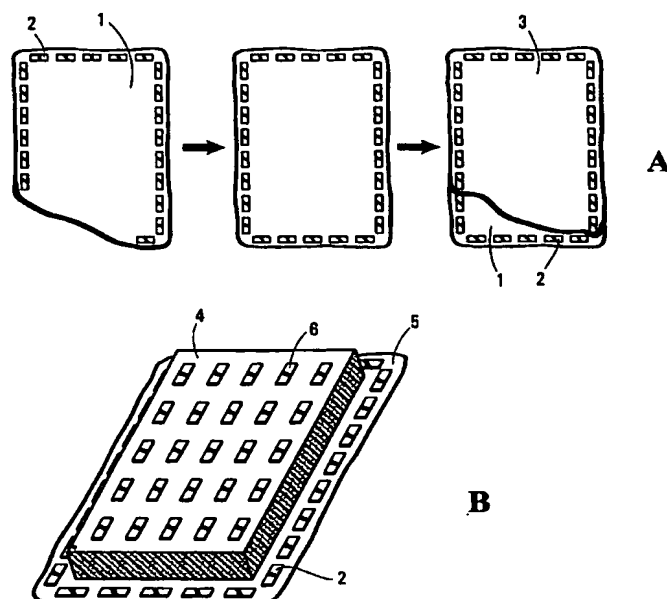
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60/396,004 16 July 2002 (16.07.2002) US
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— with international search report

[Continued on next page]

(54) Title: METHOD FOR PREPARING ENGINEERED TISSUE



(57) Abstract: A method for preparing a human or animal tissue by applying a compressive force to a stack of sheets of living tissue thereby inducing adjacent layers to fuse or adhere to each other. The force is applied in direction normal to the surface of the tissue. A multi-layer tissue produced by the method described above can also possess at least two different types of sheets and/or consist essentially of between two and twelve sheets of living tissue. The method can also be used to prepare a planar tissue that can further be incorporated in a multi-layer tissue construct. The methods and tissues described herein are useful for the preparation of engineered tissues.



— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/03/01079

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N5/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 31226 A (BADYLAK STEPHEN F ;CHENG BOYLE (US); KOKINI KLOD (US); PATEL UMESH) 10 October 1996 (1996-10-10) the whole document especially abstract page 3, line 1 -page 4, line 20 page 10, line 14 -page 11, line 8 page 14, line 10 -page 15, line 8 claims 1-26; figures 1-3 ---	1-19,25
X	WO 97 37613 A (LOWER JERRY L ;DUNN MICHAEL D (US); MAY THOMAS C (US); DEPUY ORTHO) 16 October 1997 (1997-10-16) figure 12 page 6, line 9 -page 9, line 24; claims 1-36 --- -/-	1-19,25

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
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19 November 2003

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 05262 A (BEREITER HAHN JUERGEN ;BERND AUGUST (DE)) 4 February 1999 (1999-02-04) abstract page 3, line 26, last paragraph -page 4, line 21; claims 1-6 ---	1-19,25
Y	LOPEZ VALLE C A ET AL: "Peripheral anchorage of dermal equivalents" BRITISH JOURNAL OF DERMATOLOGY, vol. 127, no. 4, 1992, pages 365-371, XP009021181 ISSN: 0007-0963 cited in the application abstract Discussion ---	5-7, 10-25
Y	WO 00 69355 A (ALTMAN GREGORY) 23 November 2000 (2000-11-23) page 5, line 20 -page 19, line 13 ---	5-7, 10-25
P,X	WO 03 007795 A (ALTERTEK BIO INC ;EDWARDS LIFESCIENCES CORP (US)) 30 January 2003 (2003-01-30) the whole document especially page 17, line 25 -page 20, line 5; figures 4-14 ---	1-25
P,X	WO 03 045458 A (BERGERON FRANCOIS ;GRENIER GUILLAUME (CA); LAROCHE DANIELLE (CA);) 5 June 2003 (2003-06-05) cited in the application page 2, line 1 - line 11 page 7, line 10 - line 25; figures 1,7,8; example 2 ---	1-25
A	YE Q ET AL: "Tissue engineering in cardiovascular surgery: new approach to develop completely human autologous tissue" EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY, SPRINGER VERLAG, BERLIN, DE, vol. 17, April 2000 (2000-04), pages 449-454, XP002959353 ISSN: 1010-7940 cited in the application abstract page 453, column 1, line 7 -page 454, last paragraph --- -/--	1-25

INTERNATIONAL SEARCH REPORT

International Application No

PCT/03/01079

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>L'HEUREUX N ET AL: "A COMPLETELY BIOLOGICAL TISSUE-ENGINEERED HUMAN BLOOD VESSEL"</p> <p>FASEB JOURNAL, FED. OF AMERICAN SOC. FOR EXPERIMENTAL BIOLOGY, BETHESDA, MD, US, vol. 12, 1998, pages 47-57, XP002942845</p> <p>ISSN: 0892-6638</p> <p>cited in the application abstract</p>	1-25
A	<p>KIM B-S ET AL: "CYCLIC MECHANICAL STRAIN REGULATES THE DEVELOPMENT OF ENGINEERED SMOOTH MUSCLE TISSUE"</p> <p>NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 17, no. 10, October 1999 (1999-10), pages 979-983, XP001145976</p> <p>ISSN: 1087-0156</p> <p>the whole document</p>	1-25
A	<p>KEIICHI KANDA ET AL: "MECHANICAL STRESS INDUCED CELLULAR ORIENTATION AND PHENOTYPIC MODULATION OF 3-D CULTURED SMOOTH MUSCLE CELLS"</p> <p>ASAIO JOURNAL, J.B.LIPPINCOTT CO., HAGERSTOWN, MD, US, vol. 39, no. 3, 1 July 1993 (1993-07-01), pages M686-M690, XP000412635</p> <p>ISSN: 1058-2916</p> <p>cited in the application abstract</p> <p>Discussion</p>	1-25

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/CA 03/01079

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-4, 8, 9 (complete) 5-7, 10-19 (partial)

a method for preparing a human or animal tissue, comprising fusing adjacent layers of tissue by applying a compressive force normal to their surface.

2. Claims: 20-25 (complete) 5-7, 10-19 (partial)

a method for preparing a planar human or animal tissue, comprising anchoring a maturing cultured tissue with adjustable anchor means.

INTERNATIONAL SEARCH REPORT

national patent family members

International Publication No

PCT/CA 01/01079

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9631226	A	10-10-1996	US 5711969 A	27-01-1998
			AU 690455 B2	23-04-1998
			AU 5536096 A	23-10-1996
			CA 2211727 A1	10-10-1996
			EP 0821590 A1	04-02-1998
			JP 3061643 B2	10-07-2000
			JP 10506125 T	16-06-1998
			WO 9631226 A1	10-10-1996
			US 5955110 A	21-09-1999
			US 5885619 A	23-03-1999
WO 9737613	A	16-10-1997	US 5788625 A	04-08-1998
			EP 0921769 A1	16-06-1999
			JP 2000506408 T	30-05-2000
			WO 9737613 A1	16-10-1997
			US 2001002446 A1	31-05-2001
			US 2001023373 A1	20-09-2001
			US 6176880 B1	23-01-2001
			US 5922028 A	13-07-1999
WO 9905262	A	04-02-1999	DE 19732194 C1	27-08-1998
			AU 9067898 A	16-02-1999
			WO 9905262 A2	04-02-1999
WO 0069355	A	23-11-2000	US 6287340 B1	11-09-2001
			CA 2371025 A1	23-11-2000
			EP 1185211 A1	13-03-2002
			JP 2002543916 T	24-12-2002
			WO 0069355 A1	23-11-2000
			US 2002062151 A1	23-05-2002
WO 03007795	A	30-01-2003	WO 03007795 A2	30-01-2003
			US 2003027332 A1	06-02-2003
WO 03045458	A	05-06-2003	WO 03045458 A1	05-06-2003